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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,014	REMACLE ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,9,10,12-38,40,42,44 and 45* is/are pending in the application.

4a) Of the above claim(s) *24-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,9,10 and 12-23,38, 40, 42, 44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 1, 2, 4, 9, 10, 12-38, 40, 42, 44 and 45 are pending. Claims 1, 2, 4, 9, 10, 12-23, 38, 40, 42, 44 and 45 are under examination. Claims 24-37 are withdrawn as directed to non-elected subject matter. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Response to Amendment

2. The declaration filed on March 13, 2006, under 37 CFR 1.131 is sufficient to overcome the Anthony reference.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997), in view of Bamdad (USPN 6,541,617).

Regarding Claims 1, 10, 38, 42 and 45, Guschin teaches a method for identifying and/or quantifying an organism or part of an organism in a sample by detecting a nucleotide sequence specific of said organism, wherein said specific nucleotide sequence presents a homology higher than 60% with at least 4 other homologous nucleotide sequences from other organisms comprising:

a) amplifying or copying said specific nucleotide sequence into target nucleotide sequence using primer pairs which are capable of amplifying at least two of said homologous nucleotide sequences from other organisms (see p. 2398, first sentence under Cloning of 16S rDNA and invitro production of RNA transcripts, where Guschin uses two primers to amplify 16S rDNA sequences form DNA extracted from five different species of bacteria. See also p. 2401 col. 2 first three sentences of the fourth paragraph);

b) contacting said target nucleotide sequence with single-stranded capture nucleotide sequences (see Table 1, where the array contains at least 9 capture nucleotide sequences including sequences specific for *Nitrobacter*, *Nitrosomonas* and *Nitrosovibrio*-like rDNA, see also p. 2401 col. 2 first three sentences of the fourth paragraph),

said single-stranded capture nucleotide sequences being covalently bound in an array to an insoluble solid support (see p. 2398 col. 2 under Microchip fabrication, where oligonucleotides were coupled to polyacrylamide gel pads). wherein said array comprises at least 4 different bound single-stranded capture nucleotide sequences/cm^2 of solid support surface (see p. 2398 col. 2 under Microchip fabrication, where the gel pads were either 60 by 60 by 20 μm or 100 by 100 by 20 μm and were spaced 120 or 200 μm apart, respectively. Even with the larger sized gel pads, this would equate to 1 gel pad (i.e. one specific single-stranded capture nucleotide sequence) per 300 μm. Since 1 cm = 10,000 μm, up to 33 by 33 (i.e. 1089) single-stranded capture nucleotide sequences per cm^2 of solid support surface would be attained.

wherein said stranded capture nucleotide sequences comprise a nucleotide sequence of about 15 to about 40 bases which is able to specifically bind to said target nucleotide sequence without binding to said at least 4 homologous nucleotide sequences (See table 1, p. 2398. The probes are all within the size range of about 5 to about 60 bases. See also figure 1. Note that while figure 1 appears to show some cross-hybridization of the *Nitrosovibrio* target nucleic acid to the *Nitrosomonas* probe, Guschin teaches on p. 2399, col. 2, lines 8-14:

> "In a like manner, the 16S rRNA of *Nitrosovibrio tenuis* hybridized to *Nitrosomonas* (Nsm156) at 10°C but was reduced to near background (compared to NonBac338) following the 40°C wash. A more complete correction for differences in stabilities of duplexes can be carried out by measuring the equilibrium or nonequilibrium melting curves for all microchip elements"

); and

detecting specific hybridization of said target nucleotide sequence to said capture nucleotide sequences (See p. 2398, col. 2, *Hybridization and image analysis*. See also figure 1).

Guschin et al. do not teach the use of a spacer that is at least 40 bases in length.

However, Bamdad teaches "for efficient hybridization of nucleic acids on a surface, the hybridization should occur at a distance from the surface i.e., the kinetics of hybridization increase as a functions of the distance from the surface" (col. 17, ln. 9-13). Bamdad teaches that

the closest nucleotide of the nucleic acid can be positioned at least 500 Angstroms from the surface (i.e., the spacer can be a polynucleotide up to 500 Angstroms or 50 nm long) (col. 17, ln. 18-2 1). Bamdad meets the limitation of at least 40 bases in length as 40 bases is equivalent to 13.6 nm which falls within the teaching of 500 Angstroms or 50nm long). It is also noted that Bamdad teaches using arrays (col. 10, ln. 20-31, for example).

In view of the teachings of Bamdad, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Guschin so as to have used a spacer of at least 40 bases in length. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin in order to have achieved the benefits stated by Bamdad of increasing the kinetics of hybridization, thus providing a more efficient means of hybridization/detection.

Regarding Claim 2, Guschin et al. teach the amplified nucleotide sequence is DNA (see p. 2398, first sentence under Cloning of 16S rDNA and invitro production of RNA transcripts, where Guschin uses two primers to amplify 16S rDNA sequences form DNA extracted from five different species of bacteria).

Regarding Claims 9 and 40, Guschin et al. teach the density of the capture nucleotide sequence bound to the surface at a specific location is more than about 10-100 fmoles per cm^2 of solid support surface (see p. 2398 col. 2 under Microchip fabrication, where Guschin teaches that 0.5 to 1 nl of oligonucleotide solution (at a concentration of 100 pmol/ml) was applied to each gel element. This equates to 0.05 to 0.1 fmol applied per gel element. For the 100 by 100 μm gel elements, this amount of probe equates to 500-1000 $fmol/cm^2$).

Regarding Claim 13, Bamdad teaches the insoluble solid support is a glass (col. 9 line 60).

Regarding Claims 16, Guschin et al. teach the solid support also bears capture nucleotide sequences specific of the homologous sequences specific for the binding with the homologous

target nucleotide sequence together with a consensus sequence able to bind to said target nucleotide sequence and to said at least 4 homologous nucleotide sequences (see table 1, p. 2398. The probes are all within the size range of about 5 to about 60 bases. See also figure 1. Note that while figure 1 appears to show some cross-hybridization of the *Nitrosovibrio* target nucleic acid to the *Nitrosomonas* probe, Guschin teaches on p. 2399, col. 2, lines 8-14:

> "In a like manner, the 16S rRNA of *Nitrosovibrio tenuis* hybridized to *Nitrosomonas* (Nsm156) at 10°C but was reduced to near background (compared to NonBac338) following the 40°C wash. A more complete correction for differences in stabilities of duplexes can be carried out by measuring the equilibrium or nonequilibrium melting curves for all microchip elements"

4. Claims 15and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997), in view of Bamdad (USPN 6,541,617), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Vannuffel et al. (WO 99/16780, cited in the IDS).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the *FemA* gene of Staphylococci species.

However, Vannuffel teaches the detection of the *FemA* gene of *Staphylococci* species is advantageous in detecting and diagnosing staphylococcal infections and for determining drug resistance (see abstract, and pages 1-5, 8-13 and Examples 1-7). Vannuffell teaches the detection of several *Staphyloloccal* species, such as *S. hominis, S. saprophyticus, S. epidermidis* and *S. haemolyticus* (pg. 4), and other gram-positive bacteria (pgs. 5 and 10).

Accordingly, in view of the teachings of Vannuffel, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Guschin and Bamdad so as to have identified and/or quantified the *FemA* sequence of *Staphylococcal* species. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of providing an effective

means of detecting specific species of the *Staphylococci* genus for use in diagnosing staphylococcal infections or for determining drug resistance.

5. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997) in view of Bamdad (USPN 6,541,617), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Boon et al. (USPN 6,488,932).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the MAGE family.

However, Boon teaches that is advantageous to detect individual sequences that belong to the MAGE family (which are closely related) for the diagnosis of tumors, (See Fig. 4 and cols. 3-8, for example).

Accordingly, in view of the teachings of Boon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Guschin and Bamdad so as to detect a sequence belonging to the MAGE family. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of providing an effective means of diagnosing a tumor.

6. Claims 4, 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997) in view of Bamdad (USPN 6,541,617), as applied to Claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Apple et al. (USPN 5,451,512).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the HLA-A family.

However, Apple teaches that is advantageous to detect individual sequences that belong to the HLA-A family (which are closely related) to help determine potential transplantation donors, thus aiding in minimizing the risk of transplantation rejection. (See cols. 1-8, for

example). Regarding Claims 4 and 14, Apple teaches the amplified nucleotide sequences can be mRNA first reverse transcribed into cDNA (see cols. 4-7, for example).

Accordingly, in view of the teachings of Apple, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Guschin and Bamdad so as to detect a sequence belonging to the HLA-A family. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of minimizing the risk of transplantation rejection.

7. Claims 12 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al (1997) as applied to claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45 above, and further in view of Martineau et al (2000).

The teachings of Guschin and Bamdad are presented above. The references do not teach using primers other than the primers capable of amplifying or copying multiple homologous sequences, primers/probes to detect antiobiotic resistance, or primers/probes to detect the specific microorganisms.

Martineau teaches a method comprising amplifying and detecting antibiotic resistance genes, as well as bacterial 16S rRNA and *Staphylococcus areus* and *Staphylococcus epidermidis* specific targets in multiplex PCR (see figure 1). Martineau uses a primer pair capable of amplifying multiple homologous genes (16S rDNA) from a variety of bacterial species, including *Staphylococcus, Enterococcus,* and *Streptococcus* (see figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention of the instant application was made to combine the multiplex PCR, using primers capable of amplifying 16S rDNA from all bacterial species as well as primers to detect antibiotic resistance genes (as taught by Martineau) with the array method of Guschin in order to achieve

simultaneous identification of a bacterial pathogen as well as the antibiotic resistance profile of the pathogen. Further motivation to combine these teachings is provided by Martineau:

> "In the clinical setting, the simultaneous identification of the bacteria and determination of its susceptibility to antibiotics generally require 48 h. Yet in the choice of empiric antibiotic therapy for suspected staphylococcal sepsis, the clinician must know rapidly which species is involved and its susceptibility to antiobiotics." (page 237, column 1, last paragraph)

8. Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997) in view of Bamdad (USPN 6,541,617), as applied to claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Klein et al. (USPN 6,255,059).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the dopamine or histamine receptors coupled to the G genes family.

However, Klein teaches that is advantageous to detect sequences that belong to the dopamine or histamine receptors coupled to the G genes family (which are closely related) to mediate transmembrane signaling by external stimuli, endocrine function, carbohydrate metabolism, etc. (see cols. 1-4, for example)

Accordingly, in view of the teachings of Klein, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Anthony and Bamdad so as to detect a sequence belonging to the dopamine or histamine receptors coupled to the G genes family. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of mediating transmembrane signaling for many vital biological processes, such as carbohydrate metabolism.

9. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997) in view of Bamdad (USPN 6,541,617), as applied to claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Murphy et al. (WO/9405695).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the choline receptors coupled to the G genes family.

However, Murphy teaches that is advantageous to detect sequences that belong to the choline receptors coupled to the G genes family (which are closely related) for use in diagnosis of neurological, viral or endocrine pathologies. (See pgs. 12-16 and 26-34, for example).

Accordingly, in view of the teachings of Murphy, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Guschin and Bamdad so as to detect a sequence belonging to the choline receptors coupled to the G genes family. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of diagnosing neurological, viral or endocrine pathologies.

10. Claims 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al. (1997) in view of Bamdad (USPN 6,541,617), as applied to claims 1-2, 9-10, 12-13, 16-17, 38, 40, and 42-45, above, and in further in view of Waxman et al. (USPN 6,207,648).

The teachings of Guschin and Bamdad are presented above. The references do not teach the sequence to be identified belongs to the cytochrome P450 isoforms family.

However, Waxman teaches that is advantageous to detect sequences that belong to the cytochrome P450 isoforms family (e.g., 2D6 and 2C19, which are closely related) for use in treatment of cancer (see cols. 3-8, 15-25 and Examples).

Accordingly, in view of the teachings of Waxman, it would have been obvious to one of

ordinary skill in the art at the time the invention was made to have modified the method of Guschin and Bamdad so as to detect a sequence belonging to the cytochrome P450 isoforms family. One of ordinary skill in the art would have been motivated to modify the teachings of Guschin and Bamdad in order to have achieved the benefit of identifying cytochrome P450 isoforms, which can be used in developing and providing anti-cancer drugs for use in treating cancer.

Response to Arguments

11. Applicant's arguments with respect to the rejections made under 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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hgc

JEFFREY FREDMAN
PRIMARY EXAMINER
5/10/06